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Via FEDEX

15 June 2010

Monisha Harris, Chemical Review Manager
Regulatory Management Branch II
Antimicrobial Division (7510P)
Office of Pesticide Programs
US Environmental Protection Agency
One Potomac Yard (South Building)
2777 S. Crystal Drive
Arlington, VA 22202

Re: Data Call-In Response
Case # 2135
Name: Dazomet, and salts

Dear Ms. Harris:

Please find enclosed the following information on the above referenced product:

- 90-Day DCI Response
- Clarification and Data Waiver Requests.

If you have any questions or require any additional information, please feel free to contact me at (901) 272-6228.

Sincerely,

Carl F. Watson, Ph.D.
Sr. Regulatory Toxicologist

United States Environmental Protection Agency Washington, D.C. 20460

OMB Approval 2070-0174

OMB Approval 2070-0107
OMB Approval 2070-0057

DATA CALL-IN RESPONSE

INSTRUCTIONS: Please type or print in ink. Please read carefully the attached instructions and supply the information requested on this form. Use additional sheet(s) if necessary.

1. Company Name and Address	2. Case # and Name	3. Date and Type of DCI and Number
BUCKMAN LABORATORIES INC 1256 NORTH MCLEAN BLVD MEMPHIS, TN 38108	2135 Dazomet, and salts Chemical # and Name 035602 Dazomet	17-Mar-2010 GENERIC ID # GDCI-035602-29024

4. EPA Product Registration	5. I wish to cancel this product registration voluntarily	6. Generic Data		7. Product Specific Data	
		6a. I am claiming a Generic Data Exemption because I obtain the active ingredient from the source EPA registration number listed below.	6b. I agree to satisfy Generic Data requirements as indicated on the attached form entitled "Requirements Status and Registrant's Response."	7a. My product is an MUP and I agree to satisfy the MUP requirements on the attached form entitled "Requirements Status and Registrant's Response."	7b. My product is an EUP and I agree to satisfy the EUP requirements on the attached form entitled "Requirements Status and Registrant's Response."
1448-98			YES	N.A.	N.A.

8. Certification I certify that the statements made on this form and all attachments are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine, imprisonment or both under applicable law.

Signature and Title of Company's Authorized Representative Carl F. Watson, PhD Sr. Regulatory Toxicologist

9. Date 6/15/10

10. Name of Company Buckman Laboratories, Inc.

11. Phone Number (901) 278-0330

United States Environmental Protection Agency Washington, D.C. 20460

OMB Approval 2070-0174

OMB Approval 2070-0107
OMB Approval 2070-0057

REQUIREMENTS STATUS AND REGISTRANT'S RESPONSE

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4. Guideline Requirement Number	5. Study Title		PROTOCOL	Progress Reports 1	2	3	6. Use Pattern	7. Test Substance	8. Time Frame (Months)	9. Registrant Response
	Applicator Exposure Data Requirements (Antimicrobial)									
875.1200	Dermal exposure--Indoor	(7 ,8)					BB, GG, Y, X, FF, Z		24	2 (1)
875.1400	Inhalation exposure--indoor	(9 ,10 ,11)					BB, GG, Y, X, FF, Z		24	3 (2)
875.1600	Application exposure monitoring data reporting	(12)					BB, GG, Y, X, FF, Z		24	3 (2)
875.1700	Product Use Information	(34 ,35)					BB, GG, Y, X, FF, Z		24	3 (2)
	Post-Application Exposure Data Requirements (Conventional Chemical)									
875.2500	Inhalation exposure	(1 ,13 ,14)					BB, GG, Y, X, FF, Z		24	9 (3)
875.2900	Data reporting and calculations	(2)					BB, GG, Y, X, FF, Z		24	9 (3)
	Postapplication Exposure Data Requirements (Antimicrobial)									
875.2800	Description of human activity	(15)					BB, GG, Y, X, FF, Z		24	3 (2)
875.2700	Product Use Information	(3)					BB, GG, Y, X, FF, Z		24	3 (2)
	Product Chemistry Data Requirements (Antimicrobial)									

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1256 NORTH MCLEAN BLVD
MEMPHIS, TN 38108

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2135 Dazomet, and salts
Chemical # and Name 035602
Dazomet

3. Date and Type of DCI and Number
17-Mar-2010
GENERIC
ID # GDCI-035602-29024

4. Guideline Requirement Number	5. Study Title		PROTOCOL	Progress Reports 1	2	3	6. Use Pattern	7. Test Substance	8. Time Frame (Months)	9. Registrant Response
830.7050	UV/Visible absorption	(21)					BB, GG, Y, X, FF, Z	TGAI & Degr	8	3 (4)
	Residue Chemistry Data Requirements (Antimicrobial)									
860.1520	Processed food/feed(FOOD COMMODITIES)	(6)					BB, GG, Y, X, FF, Z	TEP & Met	24	9 (5)
	Terrestrial and Aquatic Nontarget Organisms Data Requirements (Antimicrobial)									
850.1025	Oyster acute toxicity test (shell deposition)	(18)					BB, GG, Y, X, FF, Z	DEGR	12	3 (4)
850.1035	Mysid acute toxicity test	(19)					BB, GG, Y, X, FF, Z	DEGR	12	3 (4)
850.1075	Fish acute toxicity test, freshwater and marine	(16 ,17)					BB, GG, Y, X, FF, Z	DEGR	12	3 (4)
	Toxicology Data Requirements (Antimicrobial)									
870.3700	Prenatal developmental toxicity study	(24 ,25)					BB, GG, Y, X, FF, Z	DEGR	24	3 (4)
870.3800	Reproduction and fertility effects	(26 ,27 ,28)					BB, GG, Y, X, FF, Z	DEGR	48	3 (4)
870.4200	Carcinogenicity	(32 ,33)					BB, GG, Y, X, FF, Z	DEGR	48	3 (4)
870.5395	Mammalian erythrocyte micronucleus test	(29 ,30 ,31)					BB, GG, Y, X, FF, Z	DEGR	8	3 (4)

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Initial to indicate certification as to information on this page (full text of certification is on page one) CTW

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1256 NORTH MCLEAN BLVD
MEMPHIS, TN 38108

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870.6200	Neurotoxicity screening battery (22 ,23)					BB, GG, Y, X, FF, Z	DEGR	8	3 (4)
870.7800	Immunotoxicity (20)					BB, GG, Y, X, FF, Z	DEGR	12	3 (4)
850.2100	Avian acute oral toxicity test (4 ,5)					BB, GG, Y, X, FF, Z	DEGR	12	3 (4)

Initial to indicate certification as to information on this page (full text of certification is on page one). CFW

Date 6/15/10

Footnotes – Clarifications and Waiver Arguments

1. The registrant is a member of the ACC AEATF, which is generating data that will address this dermal exposure data requirement.

2. The registrant intends to make an offer to the ACC Dazomet Task Force (DTF) to enter into an agreement to develop the data to address this data requirement.

3. With regard to "Post-Application Exposure Data Requirements (Conventional Chemical)", it is presumed that the Agency is differentiating between agricultural (i.e., conventional chemical) and antimicrobial use patterns of dazomet. Since the use pattern of the registrant's dazomet product is restricted to antimicrobial uses, it is apparent that this data requirement is not applicable. However, pulp & paper mill exposure potential is anticipated (by general consensus of both the registrants and EPA) to be the worst case potential exposure scenario of the various outdoor and indoor antimicrobial uses of dazomet. The proposed observational monitoring study of the inhalation potential of MITC in a pulp and paper mill to address worker exposure potential (Guideline Nos. 875.1400, 875.1600, 875.1700, 875.2700, and 875.2800) is anticipated to adequately address post-application exposure potential (Guideline Nos. 875.2500 and 875.2900) such that additional data specific to those data requirements are not warranted.

4. The registrant, via the DTF, is closely monitoring the establishment of the MITC Working Group, which is being organized by Bergeson & Campbell, P.C. located at 1203 Nineteenth Street, N.W., Suite 300, Washington, DC 20036-2401 (contact point is Lisa Campbell; phone no. 202-557-3802). It is understood that the members of the MITC Working Group are joining together to address the Product Chemistry Data Requirements (830.7050, UV/Visible absorption), the Avian and Aquatic Non-Target Organism Data Requirements (850.1025, 850.1035, 850.1075, and 850.2100), and the Toxicology Data Requirements (870.3700, 870.3800, 870.4200, 870.5395, 870.6200, and 870.7800.

   While the members of the MITC Working Group will be producing those data to support agricultural use patterns of dazomet, those same data requirements are being required to support the antimicrobial uses of dazomet. Therefore, the DTF has repeatedly approached the organizers of the MITC Working Group (Bergeson & Campbell) and expressed the antimicrobial product registrant's need, and commitment, to negotiate data citation rights with the MITC Working Group. As soon as the MITC Working Group is officially formed, a formal offer can and will be extended; a copy of that formal offer will be provided as soon as it is available. The Agency will be kept informed of the progress of this agreement to cost share to support the antimicrobial uses of dazomet.

5. The waiver argument for this data requirement is presented in Attachment 1.

ATTACHMENT 1

WAIVER REQUEST FOR A DAZOMET/MITC PAPER RESIDUE STUDY

Background

EPA has requested a paper processing study to confirm that no residues of concern of dazomet or MITC remain in paper as a result of dazomet use as a slimicide in pulp and paper mills (Revised RED p115). However, the guidance document referenced (GLN 860.1520) is for processed food and feed. It is not appropriate for a confirmatory examination of potential residue levels on finished paper goods. In its reviews, the Agency suggested that the paper making study be conducted at a level of 10X the label rate using radio-labeled dazomet. In the same memo, however, EPA stated that no dietary endpoints were chosen for dazomet or MITC on the basis that "the use pattern does not indicate potential for dietary exposure" and "Dazomet is highly water soluble and therefore will primarily remain in the water on the wet-end of the paper manufacturing process. Furthermore, when mixed in an aqueous media such as the ones used in paper manufacturing plants, dazomet will hydrolyze to form MITC. Since MITC has a high vapor pressure of 2×10^4 Pa, any MITC residue in paper will likely volatilize out into the atmosphere especially during the drying processes." (see the March 21, 2007 EPA memo, "Dazomet: Dietary Risk Assessment of Antimicrobial Uses for the Reregistration Eligibility Decision (RED) Document).

Regulatory Responsibilities

EPA is responsible for registering slimicide products under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). The 1998 Antimicrobial Regulation Technical Corrections Act (ARTCA) gave the U.S. Food and Drug Administration (FDA) jurisdiction for regulating dietary residues of food-contact slimicides under Section 409 of the Federal Food, Drug and Cosmetic Act (FFDCA). Dazomet has been approved as an indirect food additive with no dosage limitations (other than use only at levels necessary to be effective) when used as a slimicide in the manufacture of paper and paperboard that contact food (21 CFR §176.300). Thus, the purpose of conducting a paper processing study for EPA would be for use in a risk assessment to confirm that there is reasonable certainty that no harm will result from the use of dazomet as a slimicide, and not for the purpose of establishing a safe limit for dazomet or MITC. However, EPA has not established acute or chronic dietary toxicological endpoints, therefore a dietary risk assessment cannot be conducted even if a paper residue study was available.

Dietary Risk Assessment

EPA has adopted the FDA method for estimating potential dietary exposure, using the slimicide dosing rate, based on potential residues in food that comes into contact with paper made with treated slurry. The Dazomet Task Force herein is providing two different exposure estimates that show that conservative calculations result in very low potential

dietary exposure to MITC from consuming food that has come into contact with paper produced with water treated with dazomet. In the first example, we estimated dietary exposure based on the maximum dazomet treatment rate for paper production. A conversion factor of 2.2 (162.3/73.12(dazomet m.w./MITC m.w.)) was used to estimate the potential residues of MITC in paper based on the dazomet dose. In the second example, the value observed for MITC in paper fresh off the rollers in the Finnish study (MRID # 47683701) was used to estimate potential dietary exposure. For both examples, we used the FDA method for estimating dietary exposure set forth by EPA in dietary risk assessments conducted for other slimicides. The FDA method is described below.

FDA Model for Estimating the Residues of Pesticides Used as Slimicides on Food Contact Paper and Paperboard

The FDA model is the worst case scenario for the dazomet slimicide use and assumes that all of the residue present in treated paper will transfer to food that contacts the paper. The FDA model assumes that the dazomet/MITC partitions between the paper pulp and the slurry water during the paper making process. That is, it is reasonable to assume that the MITC partitions into the water fraction in the paper-making process. Consequently, a portion of the MITC is "lost" in the water squeezed from the paper slurry. The FDA model[1] is used to assess the residue level of MITC that will be present in treated paper from the slimicide use and that could migrate into food exposed to the treated paper.

FDA default assumptions:

- Prior to entering the driers, the pulp slurry is 33% pulp and 67 % water.
- The standard basis weight for paper is that the paper weighs 50 mg./in^2.
- Finished paper (after paper making) contains approximately 92% pulp and 8% water.
- Food mass to surface area of treated paper is 10 gm. food /in^2 (that is, 10 grams of food will contact each square inch of the treated paper).
- There is 100% migration of the MITC from the treated paper into food (This is the FDA worst case assumption). The consumption factor is 10% (this is the fraction of the daily diet that is expected to contact the specific packaging material, in this case untreated paper, according to the FDA guidance document for indirect additives).
- The daily average food consumption for adults is 3,000 g/food and the average body weight is 60 kg for females and 70 kg for males.

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[1] FDA. 2002. "Recommendations For Chemistry Data For Indirect Food Additive Petitions" Food and Drug Administration. April 10, 2002.

• The daily average food consumption for children is 1500 g/food and the average body weight is 15 kg.

Example 1: Dazomet/MITC calculations for slimicide use based on application rate:

Maximum Treatment Rate

The maximum application rate is 0.63 lbs dazomet per ton of paper produced (Hercules-Slimetrol which contains 21% dazomet, is applied at a maximum rate of 3 lbs product/ton paper produced).

The paper slurry is 1% paper pulp (from which the paper will be produced), which is equivalent to 0.63 dazomet./200,000 lbs of paper slurry or 3.15 ppm dazomet in the paper slurry. The calculations are shown below:

0.63 lb dazomet/2000 lbs of finished paper.

Pulp paper is 1% of the paper slurry (the water/paper pulp mixture).

2000 lbs paper pulp/0.01(percentage of pulp in the slurry) = 200,000 lbs of slurry.

0.63 lb dazomet/200,000 lbs of slurry = **3.15 ppm dazomet in the paper slurry**.

Concentration in paper pulp

The concentration of active ingredient (a.i.) in the pulp prior to entering the driers is: (Application rate) x (water/pulp ratio)

(3.15 µg. a.i./gm of pulp slurry) (0.67 gm water/0.33 gm pulp) = **6.4 µg a.i./gm pulp**.

Concentration in food

(µg. of a.i./gm of pulp) (gm of pulp/gm of paper) (basis weight of paper) (food mass to surface area)

(6.4 µg a.i /gm pulp) (0.92 gm pulp/gm of paper) (0.05 gm/in.^{2}) (1 in.^{2}/10 gm food) = **0.029 µg of dazomet./gm food**.

Dazomet rapidly breaks down into MITC, therefore a conversion factor of 2.22 based on the ratio of the molecular weight of dazomet (162.3) to the molecular weight of MITC (73.12) is applied to the calculated residue level of dazomet in food to estimate the potential worst-case residue level of MITC in food.

(0.029 µg of dazomet./gm food)(2.2) = 0.065 µg MITC/gm food

Estimated Dietary Exposure

Using a Consumption Factor of 0.1[1] for uncoated paper, the concentration of MITC in the daily diet is then:

0.065 µg MITC/gm of food x 0.1 = 0.0065 µg MITC/per gm food

Estimated Daily Intake (EDI) (Adult) = (0.0065 µg MITC/gm)(3000 g food)

Adult EDI = 19.6 µg MITC/day

Adult Daily Dietary Dose = (19.6 µg MITC/day)/70 kg body weight (BW)

= 0.28 µg MITC/kg BW/day

= 0.00028 mg MITC/kg BW/day

Estimated Daily Intake (EDI) (Child) = (0.0065 µg MITC/gm)(1500 g food)

Child EDI = 9.79 µg MITC/day

Child Daily Dietary Dose = (9.79 µg MITC/day)/15 kg body weight (BW)

= 0.65 µg MITC/kg BW/day

= 0.00065 mg MITC/kg BW/day

Example 2: MITC Estimated Dietary Exposure Based on Residues observed in Paper in the Finnish Study.

Concentration in paper

In the Finnish study, paper from rolls at the end of the processing line were analyzed for MITC content. Residues in freshly made paper were detected at 0.93 and 0.86 µg MITC/kg paper, which is equivalent to < 0.001 µg/g paper.

Concentration in food

(0.001 µg. of a.i./g of paper) (basis weight of paper) (food mass to surface area)

(0.001 µg a.i /g pulp) (0.05 gm/in.^{2}) (1 in.^{2}/10 gm food) = **0.000005 µg of MITC/g food**.

Estimated Dietary Exposure

Using the FDA Consumption Factor of 0.1 for uncoated paper, the concentration of MITC in the daily diet is then:

0.000005 µg MITC/g of food x 0.1 = 0.0000005 µg MITC/per g food

Estimated Daily Intake (EDI) (Adult) = (0.0000005 µg MITC/g)(3000 g food)

Adult EDI = 0.0015 µg MITC/day

Adult Daily Dietary Dose = (0.0015 µg MITC/day)/70 kg body weight (BW)

= 0.00002 µg MITC/kg BW/day

= 0.00000002 mg MITC/kg BW/day

Estimated Daily Intake (EDI) (Child) = (0.0000005 µg MITC/gm)(1500 g food)

Child EDI = 0.00075 µg MITC/day

Child Daily Dietary Dose = (0.00075 µg MITC/day)/15 kg body weight (BW)

= 0.0.00005 µg MITC/kg BW/day

= 0.00000005 mg MITC/kg BW/day

Toxicological Endpoints

Dietary studies have not been conducted for MITC or dazomet because EPA expects that the potential for dietary exposure from registered uses is extremely small. There are two oral gavage studies available that were conducted with MITC. A three-month study conducted with mice that resulted in a NOAEL of 0.7 mg/kg/day, and a chronic dog study that resulted in a NOAEL of 0.4 mg/kg/day. [2] A 100x uncertainty factor was applied for intra- and interspecies variability. Additional uncertainty factors should not be applied because the use of an oral gavage study in place of a dietary study represents a very conservative approach. The worst-case Reference Dose (RfD) of 0.004 mg/kg bw/day was used for risk assessment purposes.

Summary and Conclusions

The following summary table contains estimated dietary exposure and risk based on the maximum application rate (Method 1) compared to the measured MITC in paper when it comes off the end of the line (Method 2). Both methods utilize FDA's model for estimating residues in food that comes into contact with treated paper, and includes the assumption that 100% of the residue will migrate from paper to food.

Table 1. Maximum Estimated Daily Intakes (EDI), Daily Dietary Doses (DDD) and RfD and Estimated Dietary Risk from MITC resulting from the use of Dazomet as a Slimicide in Paper Mills.

	EDI (µg/day)	DDD (mg/kg/day)	% RfD
Method 1: Maximum Application Rate, No Volatilization of MITC			
Adult Males	19.6	0.00028	7%
Adult Females	19.6	0.00032	8%

[2] These oral gavage studies are summarized in the report, "Risk Characterization Document for Methyl Isothiocyanate (MITC) Following the Agricultural Use of Metam Sodium." Medical Toxicology Branch, Department of Pesticide Regulation, California Environmental Protection Agency, July 25, 2003 http://www.cdpr.ca.gov/docs/risk/rcd/mitc_sb950.pdf

Children	9.8	0.00065	16%
Method 2: Measured MITC in Paper			
Adult Males	0.0015	0.00000002	<0.01%
Adult Females	0.0015	0.000000025	<0.01%
Children	0.00075	0.00000005	<0.01%

The primary reason that estimated dietary exposure based on the application rate is so much higher than measured residues is because MITC is extremely volatile and most of it is removed during the paper-making process. However, these estimates demonstrate that even if all of the dazomet applied is converted to MITC using a conversion factor of 2.2 based on molecular weight of the two compounds, and none of it volatilizes, potential dietary exposure is very small and represents a small percentage of a very conservative RfD.

In addition, the MITC residues measured in paper in the Finnish study were 0.93 and 0.86 ug/kg paper, which is equivalent to < 1 ppb MITC. Although the application rate calculated for the Finnish study (0.11 lbs dazomet/ton paper) was lower than the maximum application rate (0.63 lbs dazomet/ton paper), the measured residues in paper were three orders of magnitude lower than the 200 ppb level in paper that EPA generally considers not to be of concern. If MITC in paper increased proportionately to the application rate, then the highest application rate would result in approximately 6 ppb in paper, and would still be two orders of magnitude lower than the 200 ppb level of no concern.

For these reasons, the Dazomet Task Force respectfully requests for EPA to waive the requirement for a paper processing.